Long duration head-down tilt bed rest studies: safety considerations regarding vision health

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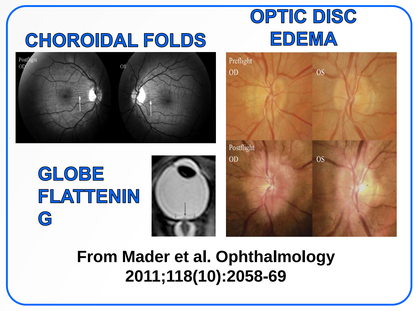
BACKGROUND

- Visual symptoms reported in astronauts returning from long duration missions in low Earth orbit are thought to be related to fluid shifts within the body due to microgravity exposure.



- Because of this possible relation to fluid shifts, safety considerations have been raised regarding the ocular health of head-down tilt (HDT) bed rest subjects.

PURPOSE

To perform vision monitoring in bed rest (BR) subjects in order to evaluate the safety of HDT with respect to vision health.

METHODS

- An integrated, multidisciplinary 70-day -6° head-down tilt
- Two experimental groups: exercisers and controls
- Vision tests: Pre-BR 2 Baselines (Office; BR -10,-3); BR, weekly (FARU, or office); post-BR, 2 (Office; BR +2, +8)

NASA Flight Analogs Research Unit (FARU) Standarized Conditions

- ✓ Subject to rest in bed **at all times**
- ✓ Monitoring by a subject monitor and an in room camera **24 hours a day**
- ✓ Daily measurement of vital signs, body weight, fluid intake and fluid output
- ✓ No napping permitted between 6:00 am and 10:00 pm
- ✓ Standardized diet

METHODS

- Ophthalmoscopic evaluation of the retina and the optic disc (0° BR, pre- and post-BR)
- Stereophotographs of the retina and the optic disc (-6° BR, pre and post BR
- Cycloplegic refraction and Best Corrected Visual Acuity (BCVA, at all time points)
- Intraocular pressure (IOP): 4 measurements per eye. Goldmann (pre- and post-BR); iCare (-6° BR, at all time points; IOP measured with Tonopen in 5 subjects)

- SPECTRAL-DOMAIN OCT (pre-, mid, and post-BR):
  - ✓ Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA; vers. 5.0):
    - ➢ Optic disc parameters
    - ➢ Average Retinal Nerve Fiber Layer (RNFL) thickness
    - ➢ Macular Cube average thickness
  - ✓ Spectralis OCT (Heidelberg Engineering, GmbH, Heidelberg, Germany; vers. 5.1.3.0):
    - ➢ Average RNFL thickness and total retinal thickness (macular, peripapillary)
  - ✓ iVue portable OCT device (Optivue, Inc., Fremont, CA): permitted one in bed-phase measure at BR38 at -6 degrees

RESULTS

- Results correspond to 9 subjects who completed the C11 study as of August 15, 2012.
- A group of 4 subjects (group A) had OCT measures with Cirrus/Spectralis; a group of 5 subjects (group B) had OCT measures with iVUE.
- Findings for the following tests were all reported as normal in each testing session for every subject: modified Amsler grid, red dot test, confrontational visual fields, color vision and fundus photography.
- Near and far visual acuity increased during the course of the study, but this may be considered an artifact of test learning.
- Intraocular pressure slightly increased during the bed rest phase (p=0.059) and to a less extent, at post-bed rest with respect to baseline (p=0.046) *(Figure 1)*

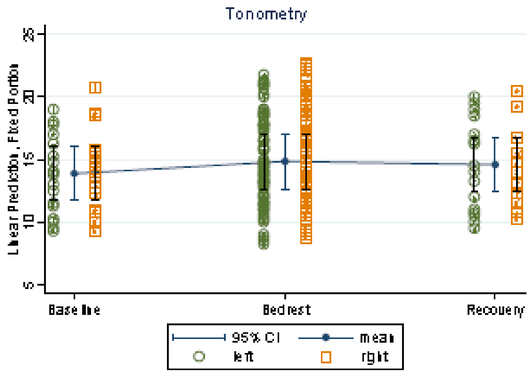
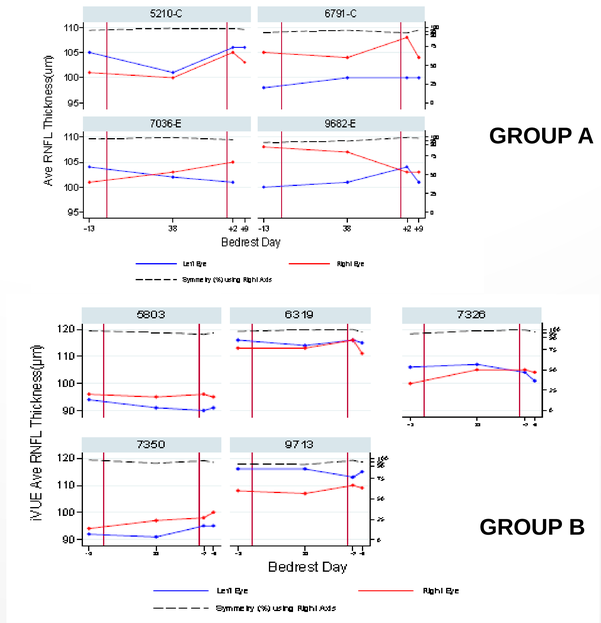


Figure 1-Intraocular pressure in pre-, in- and post bed rest. Measures were taken at days: BR-5, BR38, BR+2

- While IOP subtly increased with respect to baseline, no changes were observed in RNFL thickness pre versus during or post bedrest *(Figure 2)*

Figure 2-OCT measures for average retinal nerve fiber layer (RNFL) for each individual in GROUP A (Cirrus) and GROUP B (iVUE). No statistical tests were performed on these data due to the small n (n=4 and n=5, respectively)



RESULTS

- The association between the average RNFL thickness and IOP measurements was investigated using pre, during and post bed rest data altogether by Kendall's Tau-b, with adjustments to SE for repeated measures. This rank-correlation is particularly desired for small sample sizes or non-normally distributed data (Figure 3)

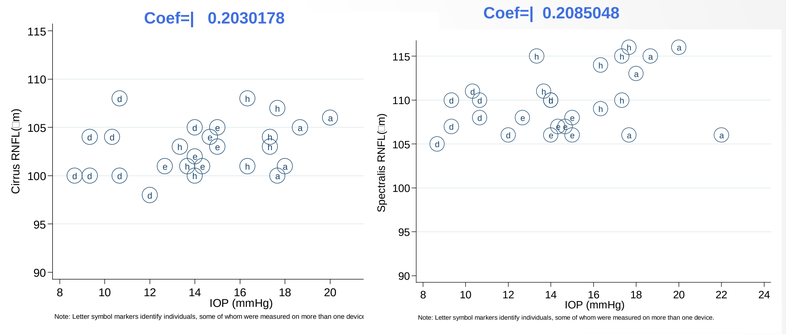


Figure 3- Kendall's Tau-b Association between IOP and average RNFL with various OCT instruments

- This analysis showed a significant positive association between IOP and average RNFL thickness measured by Cirrus (p=0.028) and nearly significant when measured by Spectralis (p=0.079). In contrast, there was no association between IOP and RNFL thickness as measured with the iVUE instrument (p=0.904)

CONCLUSIONS

- -6° head-down tilt BR produced a subtle increase in IOP
- More research is needed to evaluate ocular changes and to better characterize patterns of IOP changes related to long-duration BR, in particular in the early days of bed rest, and the recovery period
- While the analysis performed on the n=9 subjects reported here is preliminary, an association was observed with Cirrus and Spectralis instruments and not with iVUE, suggesting that measurements with iVUE may introduce larger variability
- Other parameters (e.g. ICP, venous congestion) might be involved in explaining the positive association between IOP and RNFL thickness

SUPPORT

NASA Flight Analogs Project, 516724.03.04.01